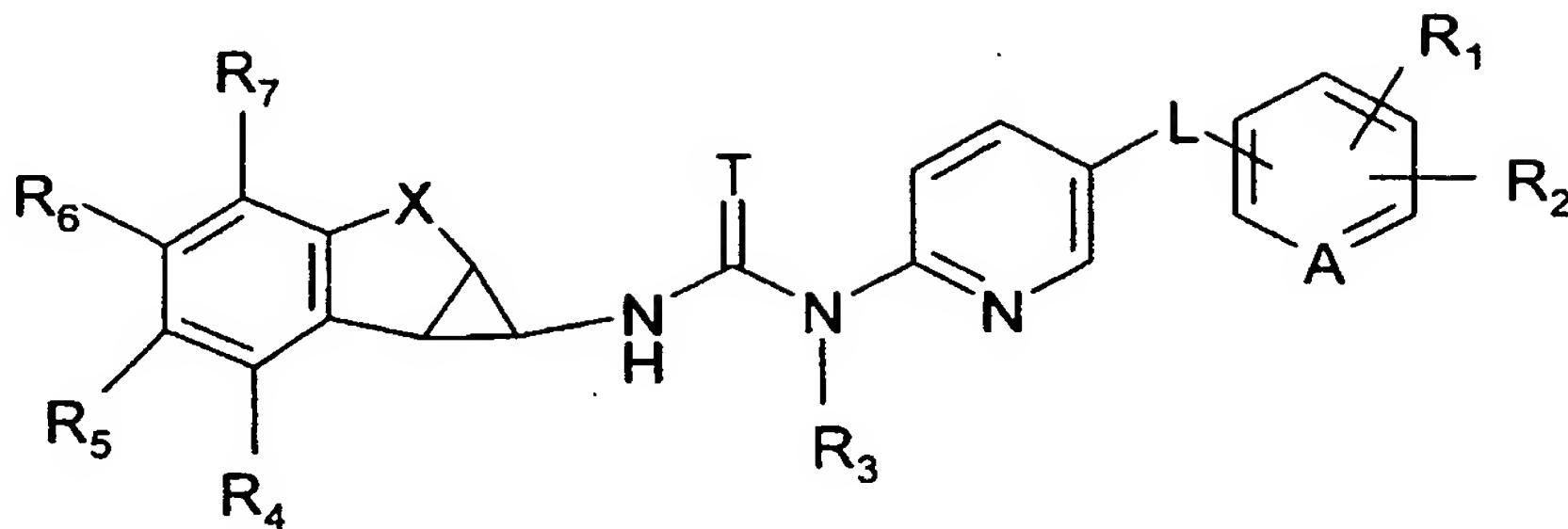


Claims

1. A compound of the formula Z:



where;

5 A is CH or N;

R₁ is a substituent to a carbon atom in the ring containing A selected from -S(=O)_pR_a,

where R_a is -C₁-C₄ alkyl, -OR_x, -NR_xR_x, -NHNR_xR_x, -NHNHC(=O)OR_x, -NR_xOH;

10 -C(=O)-R_b,

where R_b is -C₁-C₄-alkyl, OR_x, -NR_xR_x, -NHNR_xR_x, -NHC₁-C₃-alkyl-C(=O)OR_x

-NR_xR_c,

where R_c is H, C₁-C₄ alkyl, -NR_xR_x; -C(=O)R_d, -CN, S(=O)_pR_x

15

where R_d is R_d is C₁-C₄-alkyl, -OR_x, -NR_xR_x

-C₁-C₃-alkyl-O-C₁-C₃alkylC(=O)OR_x,

-C₁-C₃-alkyl-COOR_x;

-C₁-C₃alkyl-OR_x

20 -(O-C₁-C₃alkyl)_q-O-R_x

a 5 or 6 membered aromatic ring have 1-3 hetero atoms;

p and q are independently selected from 1 or 2;

R_x is independently selected from H, C₁-C₄ alkyl or acetyl; or a pair of R_x can together with the adjacent N atom form a pyrrolidine, piperidine, piperazine or

25 morpholine ring;

R₂ is a substituent to a carbon atom in the ring containing A and is H, halo, cyano, C₁-C₄-alkyl, haloC₁-C₄-alkyl;

L is -O-, -S(=O)_r- or -CH₂-, where r is 0, 1 or 2;

R₃ is H, C₁-C₃ alkyl;

5 R₄-R₇ are independently selected from H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, haloC₁-C₆ alkyl, C₁-C₆ alkanoyl, haloC₁-C₆ alkanoyl, C₁-C₆ alkoxy, haloC₁-C₆ alkoxy, C₁-C₆ alkyloxyC₁-C₆ alkyl, haloC₁-C₆ alkyloxyC₁-C₆ alkyl, hydroxyC₁-C₆ alkyl, aminoC₁-C₆ alkyl, carboxyC₁-C₆ alkyl, cyanoC₁-C₆ alkyl, amino, carboxy, carbamoyl, cyano, halo, hydroxy, keto;

10 X is -(CR₈R₈')_n-D-(CR₈R₈')_m-;

D is a bond, -NR₉-, -O-, -S-, -S(=O)- or -S(=O)₂-;

n and m are independently 0, 1 or 2, provided that they are not both 0 when D is a bond;

R₈ and R₈' are independently H, C₁-C₃ alkyl, haloC₁-C₃ alkyl, hydroxy, or R₈ and R₈'

15 together with their adjacent C atom is -C(=O)-

R₉ is independently H, C₁-C₃ alkyl;

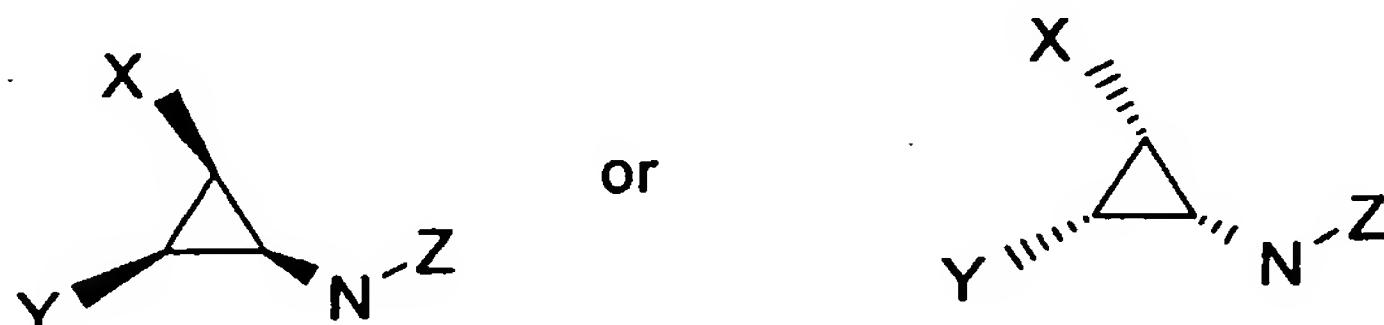
and pharmaceutically acceptable salts and prodrugs thereof;

with the proviso that R² as -C(=O)Rb is not morpholinoketo-.

2. A compound according to claim 1, wherein T is O.

20 3. A compound according to claim 1, wherein R₃ is H.

4. A compound according to claim 1, wherein the cyclopropyl moiety has an enantiomeric excess of the conformation depicted in the partial formulae:



where X is as defined, Y is the bridge to the (substituted) phenyl ring depicted in formula I and Z is bond to the (thio)urea-pyridyl moiety depicted in formula Z.

25 5. A compound according to claim 1 wherein the compound of formula Z comprises an enantiomeric excess of the isomer showing negative optical activity.

6. A compound according to claim 1, wherein D is $-O-$.
7. A compound according to claim 6, wherein n is 0 and m is 1.
8. A compound according to claim 1, wherein R_4 is hydrogen, fluoro or hydroxy.
9. A compound according to claim 1, wherein R_5 is hydrogen, fluoro, C_{1-3} alkylcarbonyl or C_{1-3} alkyloxy.
10. A compound according to claim 1, wherein R_6 is hydrogen, halo, C_{1-3} alkyloxy, C_{1-3} alkylcarbonyl, cyano or ethynyl.
11. A compound according to claim 10, wherein R_6 is hydrogen, methoxy or fluoro.
12. A compound according to claim 1, wherein R_7 is hydrogen, cyano, halo, C_{1-3} alkyloxy, or C_{1-3} alkylcarbonyl.
13. A compound according to claim 12, wherein R_7 is cyano, fluoro or acetyl.
14. A compound according to claim 1, wherein R_5 and R_6 are H and R_4 and R_7 are fluoro.
15. A compound according to claim 1, wherein R_4 is fluoro, R_5 and R_6 are H, and R_7 is cyano or acetyl.
- 25 16. A compound according to claim 1, wherein L is $-O-$.
17. A compound according to claim 1, wherein R_1 is $-S(=O)_2NR_xR_x$, $S(=O)_2C_{1-C_4}$ alkyl, or $S(=O)C_{1-C_4}$ alkyl.
18. A compound according to claim 17, wherein R_1 is $-S(=O)_2NH_2$, $-S(=O)_2NMe_2$ or $-S(=O)_2NH$ -cyclopropyl.

19. A compound according to claim 17, wherein R₁ is -S(=O)₂Me or -S(=O)Me.
20. A compound according to claim 1, wherein R₁ is -C(=O)ORx, -C(=O)NRxRx, -C(=O)NHNRxRx or -C(=O)NHCH₂COORx.
21. A compound according to claim 20, wherein R₁ is -C(=O)OH, -C(=O)OMe, -C(=O)NH₂, -C(=O)NHMe, -C(=O)NNH₂, -C(=O)NHCH₂COOH.
5
22. A compound according to claim 20, wherein R₁ is -C(=O)NRx'-N-morpholine, -C(=O)NRx'-N-piperidine, -C(=O)NRx'-N-pyrrolidine or -C(=O)NRx'-N-piperazine, where Rx is methyl, acetyl or preferably H.
23. A compound according to claim 1, wherein R₁ is -NRxRx, -N(C=O)C₁-C₄-alkyl
10 or -NHC(=O)CH₂OC₁-C₃-alkyl-COORx.
24. A compound according to claim 23, wherein R₁ is -NH₂, -NHC(=O)Me or NHC(=O)CH₂OCH₂C(=O)OH.
25. A compound according to claim 1, wherein R₁ is -C₁-C₃-alkyl-COORx;
15 -C₁-C₃alkyl-ORx, -(O-C₁-C₃alkyl)_q-O-Rx or a 5 membered ring having 1-3 hetero atoms.
26. A compound according to claim 25, wherein R₁ is carboxyethyl or a methyl ester thereof, 2-methoxyethoxyethoxy or triazolyl.
- 20 27. A compound according to claim 1, wherein R₁ is para to the ether linkage.
28. A compound according to claim 1, wherein the ring containing A is phenyl or pyrid-3-yl.
29. A compound according to claim 1, wherein R₂ is hydrogen or fluoro.
30. A compound according to claim 1 where R₂ is meta to the ether linkage.
25
31. A compound according to claim 1 denoted N-[(1S,1aR,7bR)-4,7-difluoro-1,1a,2,7b-tetrahydrocyclopropa[c]chromen-1-yl]-N'-[5-(4-(sulfonamido)phenoxy)-2-pyridinyl]urea.

32. A pharmaceutical composition comprising a compound as defined in any preceding claim and a pharmaceutically acceptable vehicle or diluent therefor.
- 5
33. A composition according to claim 32, further comprising 1 to 3 additional HIV antivirals.
- 10
34. A composition according to claim 32, further comprising a cytochrome P450 modulator, such as ritonavir.
- 15
35. Use of a compound as defined in any of claims 1-31 in the manufacture of a medicament for the prophylaxis or treatment of HIV-1 infections.
36. Use according to claim 35, wherein the HIV-1 infection is a drug escape mutant.
- 20
37. Use according to claim 36, wherein the drug escape mutant comprises the L100I and K103N mutations.